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10/748,831	12/30/2003	Richard L. Boyd	NOR-016CP2 and 286336.155	2793

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/748,831	BOYD, RICHARD L.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-34,36-43,45-55,60-63,70,71,81,83,84 and 86-88* is/are pending in the application.

4a) Of the above claim(s) *34,43,47,48,52,63,81 and 84-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-33,36-42,45,46,49-51,53-55,60-62,70,71,83,87 and 88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 10/31/08 was entered.

Claims 1-2, 4-34, 36-43, 45-55, 60-63, 70-71, 81, 83-84 and 86-88 are pending in the present application.

This application contains claims 81 and 84-86 drawn to an invention nonelected with traverse in the reply filed on 8/24/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Previously, Applicants elected the following species: (a) Leuprolide as a species of a pharmaceutical for the disruption of sex-steroid-mediated signaling to the thymus to reactivate the thymus; (b) Genetically modified hematopoietic stem cells (HSC) as a species of administered genetically modified cells to the patient; (c) IL-7 as a species of a cytokine; and (d) a gene coding for a ribozyme that cuts HIV tat as a species of a polynucleotide expressible in genetically modified cells.

Claims 34, 43, 47-48, 52 and 63 were withdrawn previously from further consideration because they are directed to non-elected species.

Accordingly, amended claims 1-2, 4-33, 36-42, 45-46, 49-51, 53-55, 60-62, 70-71, 83 and 87-88 are examined on the merits herein with the aforementioned elected species.

Response to Amendment

The rejection under 35 U.S.C. 112, first paragraph, for enablement was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated Sykes et al. (US 5,658,564; IDS) and evidenced by Fredrickson et al. (Developmental and Comparative Immunology 18:251-263, 1994; IDS) was withdrawn in light of Applicant's amendment..

The rejections under 35 U.S.C. 103(a) set forth in the previous Office Action dated 01/16/08 were withdrawn in light of Applicant's amendment.

Claim Objections

Claim 41 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This is because the limitation in claim 41 is already present in amended independent claim 27 from which claim 41 is dependent on.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 53-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is a new ground of rejection necessitated by Applicant's amendment.***

Amended claims 53-54 contain the limitation "**genetically modifying cells in vitro with a vector construct encoding and expressing a gene product that inhibits replication of human immunodeficiency virus (HIV)" and "wherein the patient is infected with a virus"**, and **the virus is selected from a specific Markush group recited in dependent claim 54**. As written, claims 53-54 encompass the specific use of genetically modifying cells containing and expressing a gene product that inhibits replication of HIV to treat a patient that is infected by any virus, not necessarily a patient infected with HIV (e.g., a patient infected with any Picornaviridae, Calviviridae, Flaviridae, Herpesviridae, Iridoviridae among others). The as-filed **specification does not have a written support for this specific embodiment as encompassed by the presently amended claims 53-54 (see at least originally claims 27 and 53-54)**. In the amendment filed on 10/31/08, Applicant failed to point out **the specific page number and/or line number of the as-filed specification** that provide the written support for the above specific claimed embodiment.

Therefore, given the lack of sufficient guidance provided by the originally filed specification, it would appear that Applicant did not contemplate or had possession of the instant broadly claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Amended claims 1-2, 4-9, 12, 14-18 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al. (US 5,658,564; IDS) and in view of Nowak, R (New Scientist 19/26, page 11, January 2, 1999; IDS), Garzetti et al. (Obstet Gynecol. 88:234-240, 1996; IDS), Mathias, JR (US 5,434,136; IDS) and evidenced by Balasubramanian (US 5,824,322; IDS submitted on 10/07/08). ***This is a new ground of rejection necessitated by Applicant's amendment.***

Sykes et al disclose at least a method of restoring or inducing immunocompetence in a host or recipient, including a human adult or a human child, said method comprises the steps of introducing into said host **any donor thymic tissue (including normal non-fetal or non-neonatal thymic tissue)**, preferably fetal or neonatal thymic tissue, so that host T cells can mature in the implanted thymic tissue; depleting, inactivating or inhibiting recipient natural killer cells or host T cell function

(e.g., introducing antibodies capable of binding to NK cells, T cells and CD4+ cells); irradiating the recipient with low dose, whole body irradiation (e.g., subletthal irradiation, col. 28, lines 47-60); a short course of high dose immunosuppressant such as cyclosporine; as well as recipient genetically modified hematopoietic stem cells expressing a donor antigen (e.g., a donor MHC gene) to facilitate tolerance to subsequent exposure to donor antigen (see at least Summary of the Invention, particularly col. 1, line 38 continues to line 35 of col. 3 and issued claims). Sykes et al also teach **the same method for treating a human at risk for an acquired immune disorder such as AIDS, patients suffering from an immunodeficiency such as a T cell deficiency, immunoincompetence resulting from a neoplastic disease or immunoincompetence resulting from a medical procedure such as chemotherapy or radiation treatment** (col. 5, line 29 continues to line 19 of col. 7; col. 14, lines 29-30; coll. 15, lines 31-39).

Sykes et al further teach that **due to the discovery that hematopoietic stem cells can be used to induce tolerance to a graft (e.g., liver, kidney, hear, endocrine glands or progenitor stem cells of various types), they disclose a method for inducing immunological tolerance in a recipient mammal**, including a human adult or a human child, of a first species to a graft obtained from a donor mammal of a second species, said method comprises prior to or simultaneous with transplantation of the graft, introducing into the recipient mammal hematopoietic stem cells of the second species; depleting, inactivating or inhibiting recipient natural killer cells or host T cell function (e.g., introducing antibodies capable of binding to NK cells, T cells and CD4+

cells); irradiating the recipient with low dose, whole body irradiation (e.g., subletthal irradiation, col. 28, lines 47-60); and a short course of high dose immunosuppressant such as cyclosporine (col. 11, line 16 continues to line 16 of col. 13; and particularly issued claims 21-24). Sykes et al disclose that although hematopoietic stem cells derived from the graft donor are preferable, hematopoietic stem cells may be obtained from other individuals or species, or from genetically-engineered completely or partially inbred donor strains (col. 27, lines 34-37).

Sykes et al do not teach specifically the use of Leuprolide, an LHRH agonist, (the elected species) in any of their disclosed methods for restoring or inducing immunocompetence in a treated host, including a human at risk for an acquired immune disorder such as AIDS or patients suffering from an immunodeficiency such as a T cell deficiency, immunoincompetence resulting from a neoplastic disease or immunoincompetence resulting from a medical procedure such as chemotherapy or radiation treatment.

However, at the effective filing date of the present application Nowak already reported that temporary chemical castration could help regenerate the damaged immune systems of people with HIV or who have had chemotherapy or bone marrow transplants. Nowak further disclosed that the work of Drs. Boyd and Sutherland demonstrated that upon castration, thymus of adult mice regained its youthful appearance within four weeks and the number of T cells produced increased to near pre-pubertal levels, suggesting that **drugs (e.g., LHRH or luteinising hormone-releasing hormone) that suppress the production of sex steroids and partially**

reverse puberty might boost the immune systems of patients with AIDS or those who gave been given immunosuppressive drugs.

At the effective filing date of the present application, Garzetti et al also taught that **a positive immunomodulating effect, particularly a significant progressive increase in natural killer (NK) cell activity was observed during the first 12 weeks of gonadotropin-releasing hormone (GnRH) agonist treatment in patients with advanced endometriosis, and they proposed GnRH agonist treatment as an adjuvant medical treatment for endometriosis** (see at least the abstract; page 239, col. 2, last paragraph).

Additionally, Mathias taught the use of GnRH analogs, **particularly Lupron or luprolide acetate due to its increased biologic activity, stability against enzymatic degradation and high binding affinity for GnRH receptors, for alleviating the debilitating symptoms of motility disorders such as systemic lupus erythematosis, autonomic neuropathies of diabetes mellitus, sclerroderma, Parkinson's disease, functional bowel disease at least via their inhibitory activity against the production of reproductive hormones** (see at least Summary of the Invention, particularly col. 3, lines 34-46 and 53-60; col. 2, lines 52-62). Mathias further disclosed that GnRH and its analogs are routinely used in the treatment of disorders of the reproductive system, including patients with endometriosis, hormone-dependent tumors such as prostatic mammary carcinomas, polycystic ovarian disease (col. 4, lines 48-62).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of invention was made to modify the teachings of Sykes et al. by also selecting and administering leuprolide to the treated host, **particularly in a patient receiving a non-neonatal or non-fetal thymic tissue (normal adult thymic tissue) or in a non-thymectomized patient (an embodiment taught by Sykes et al for inducing immunological tolerance to a graft such as liver, kidney, hear, endocrine glands or progenitor stem cells of various types due to the tolerant properties of hematopoietic stem cells)**, in light of the teachings of Nowak, Garzetti et al. and Mathias discussed above.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance immunocompetence in the treated patients, particularly in human patients that are HIV positive or having AIDS. Furthermore, it is also apparent that GnRH and its analogs such as leuprolide have been used safely in humans for various treatments. It should be noted that **an adult thymus tissue is at least in part deactivated relative to fetal or newborn thymus tissue** because atrophy of the thymus with age is a characteristic of all species which is associated with aging and the cessation of growth, and **it is already well known in the prior art that castration slows thymic involution while injection of coritcosteroid hormones accelerates thymic involution as evidenced by Balasubramanian** (col. 2, lines 1-18). Additionally, **thymus tissue from HIV infected patients is severely deactivated or has a profound thymic involution as evidenced by Balasubramanian** (col. 3, line 52 continues to line 20 of col. 4). Accordingly, the resulting modified method as set forth

above is indistinguishable from the method as claimed because it has the same method steps and starting materials.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Sykes et al., Nowak, Garzetti et al. and Mathias with evidence by Balsubramanian; coupled with a high level of skill of an ordinary artisan in the relevant art.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Amended claims 10- 11, 13, 19-33, 36-42, 45-46, 49-51, 53-55, 60-62, 70-71 and 87-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al. (US 5,658,564; IDS) and in view of Nowak, R (New Scientist 19/26, page 11, January 2, 1999; IDS), Garzetti et al. (Obstet Gynecol. 88:234-240, 1996; IDS), Mathias, JR (US 5,434,136; IDS) and evidenced by Balasubramanian (US 5,824,322; IDS submitted on 10/07/08) as applied to claims 1-2, 4-9, 12, 14-18 and 83 above, and further in view of Dropulic et al. (US 6,232,120 B1) and Bolotin et al. (Blood 88:1887-1894, 1996; IDS). ***This is a new ground of rejection necessitated by Applicant's amendment.***

The combined teachings of Sykes et al., Nowak, Garzetti et al. and Mathias with evidence by Balasubramanian were already presented above. However, none of the references teaches specifically using hematopoietic stem cells genetically modified with a gene that inhibits infection, replication or function of human immunodeficiency virus, particularly a gene coding for a ribozyme that cuts HIV tat gene (elected species); and

further treating the patient with anti-retroviral therapy, particularly highly active retroviral therapy, or a further step of administering IL-7 (the elected species) .

However, at the effective filing date of the present application Droulic et al already taught a method for inhibiting the replication of an infective replicable human immununodeficiency virus (HIV) in a cell, including a stem cell (at least col. 20, lines 46—58), in a patient or *in vivo* by contact the cell *ex vivo* which is infected or at risk of being infected with the HIV virus with a conditionally replicating recombinant viral vector encoding and expressing a ribozyme targeting a wild type HIV genome, including a triple anti-Tat ribozyme cassette, wherein the catalytic domain of each ribozyme of the triple ribozyme cassette cleaves a different site on a wild-type human HIV nucleic acid molecule (col. 15, line 56 continues to line 11 of col. 16), then return of the genetically modified cell to the patient (see at least col. 23, line 9 continues to line 53 of col. 24; issued claims, particularly claims 24 and 30). Dropulic et al further taught that treated patients could also be subjected to other conventional treatments, including administration of anti-retroviral agents such as RT inhibitors, such as ddC, zidovudine, ddI, ddA or other inhibitors that act against other HIV proteins, such as anti-TAT agents (highly active retroviral therapy); as well as administration of immunomodulators and immunostimulants such as various interleukins, CD4, cytokines, blood transfusion and cell transfusions, antifungal and antibacterial agents (col. 27, line 54 continues to line 46 of col. 28).

Additionally, at the effective filing date of the present application Bolotin et al already taught that IL-7 administration promotes thymic reconstitution and enhanced

thymopoiesis after bone marrow transplantation (BMT) and is useful in preventing post-bone marrow transplantation immune deficiency (see at least the abstract).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of the invention was made to further modify the method taught by Sykes et al., Nowak, Garzetti et al. and Mathias with evidence by Balasubramanian by further genetically modifying transplanting hematopoieitc stem cells in patients having or at risk of HIV infection with a conditionally replicating recombinant viral vector encoding and expressing a ribozyme targeting a wild type HIV genome, including a triple anti-Tat ribozyme cassette, as well as further administering IL-7 into the treated patient in light of the teachings of Dropulic et al. and Bolotin et al. as discussed above.

An ordinary skilled artisan would have been motivated to carry out the above modifications to reduce or limit wild-type HIV pathogenicity or at least to reduce HIV virus load burden in a patient having or at risk of HIV infection by the approach already successfully taught by Dropulic et al.; and the further IL-7 administration into a patient in need thereof would further enhances thymopoiesis and thereby enhancing immunocompetence in the treated patient due to the teachings of Bolotin et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Sykes et al., Nowak, Garzetti et al., Mathias with evidence by Balasubramanian, Dropulic et al. and Bolotin et al.; coupled with a high level of skill of an ordinary artisan in the relevant art.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments related in part to the above rejections in the Amendment filed on 6/16/08 (pages 15-17) have been fully considered, but they are respectfully not found persuasive for the reasons discussed below.

Applicant argues basically that the above combination of references was not used to reject claim 3 with the limitation "whose thymus has been at least in part deactivated", and therefore the instant amended claims are non-obvious over the combined references.

Firstly, it should be noted that original claim 3 was already rejected under 35 U.S.C. 102(b); and therefore it was not free of prior art. The incorporation of the limitation found in claim 3 into the instant amended claims necessitates the above new ground of rejection.

Secondly, as already stated in the above rejection it would have been obvious for an ordinary skilled artisan at the time of invention was made to modify the teachings of Sykes et al. by also selecting and administering leuprolide to the treated host, **particularly in a patient receiving a non-neonatal or non-fetal thymic tissue (normal adult thymic tissue) or in a non-thymectomized patient (an embodiment taught by Sykes et al for inducing immunological tolerance to a graft such as liver, kidney, hear, endocrine glands or progenitor stem cells of various types due to tolerant properties of hematopoietic stem cells)**, in light of the teachings of Nowak, Garzetti et al. and Mathias. An ordinary skilled artisan would have been

motivated to carry out the above modification to enhance immunocompetence in the treated patients, particularly in human patients that are HIV positive or having AIDS. Furthermore, it is also apparent that GnRH and its analogs such as leuprolide have been used safely in humans for various treatments. It is noted that **an adult thymus tissue is at least in part deactivated relative to fetal or newborn thymus tissue** because atrophy of the thymus with age is a characteristic of all species which is associated with aging and the cessation of growth, and **it is already well known in the prior art that castration slows thymic involution while injection of coritcosteroid hormones accelerates thymic involution as evidenced by Balasubramanian** (col. 2, lines 1-18). Additionally, **thymus tissue from HIV infected patients is severely deactivated or has a profound thymic involution as evidenced by Balasubramanian** (col. 3, line 52 continues to line 20 of col. 4).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Amended claims 1-2, 4-5, 7, 14-18 and 83 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62 and 64 of copending Application No. 10/749,119. ***This is a modified rejection necessitated by Applicant's amendment.***

Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are directed to a method for genetically altering a subject comprising the steps of genetically modifying cells from a recited Markush group of cells, and delivering them to the subject while the subject's thymus is undergoing reactivation by disruption of sex steroid-mediated signaling to the patient's thymus or a method for improving uptake by the thymus of a patient of genetically modified cells or exogenous cells having the specific steps recited in independent claim 83. Claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62 and 64 of copending Application No. 10/749,119 are drawn to a method for inducing tolerance in a patient to a graft from a mismatched donor, comprising the steps of depleting T cells of the patient or providing the patient with immunosuppressive therapy, reactivating the thymus of the patient and administering cells from the mismatched donor to the patient, wherein the cells being selected from the group consisting of stem cells, progenitor cells, dendritic cells, and combinations thereof.

The claims of the present application differ from the claims of the co-pending application in reciting "genetically modifying cells, wherein the cells are selected from HSC"; and "thymus is undergoing reactivation by disruption of sex steroid-meidated

signaling to the patient's thymus". The claims of the present application can't be considered to be patentably distinct over claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62 and 64 of copending Application No. 10/749,119 when the scope of independent claim 19 encompasses specifically hematopoietic stem cells (dependent claim 28) and genetically modified cells from a mismatched donor (dependent claim 60), and reactivating the thymus of the patient specifically via disruption of sex steroid-mediated signaling to the thymus (dependent claim 23); and therefore they fall within the scope of claims 1-2, 4-5, 7, 14-18 and 83 of the present application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Amended claims 1-2, 4-9, 14-18 and 83 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-30, 32-33, 36-42, 45-50, 80-82, 92-98 of copending Application No. 10/749,118. ***This is a modified rejection necessitated by Applicant's amendment.***

Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are directed to a method for genetically altering a subject comprising the steps of genetically modifying cells from a recited Markush group of cells, and delivering them to the subject while the subject's thymus is undergoing reactivation by disruption of sex steroid-mediated signaling to the patient's thymus; and a method for improving uptake by the thymus of a patient of genetically modified cells or exogenous cells having the specific steps recited in independent claim 83. Claims 29-

30, 32-33, 36-42, 45-50, 80-82, 92-98 of copending Application No. 10/749,118 are drawn to a method for treating or alleviating symptoms of an autoimmune disease in a patient having or suffering an autoimmune disease, comprising: depleting T cells in the patient; and reactivating the thymus of the patient, the thymus being reactivated by disruption of sex steroid-mediated signaling to the thymus, wherein the patient has an improved prognosis for the autoimmune disease compared to an untreated patient suffering from the autoimmune disease.

The claims of the present application differ from the claims of the co-pending application in reciting "genetically modifying cells, wherein the cells are selected from HSC..... and administering them to the patient". The claims of the present application can't be considered to be patentably distinct over claims 29-30, 32-33, 36-42, 45-50, 80-82, 92-98 of copending Application No. 10/749,118 when the scope of independent claim 29 encompasses specifically the step of further administering cells to the patient, wherein the cells are stem cells, including hematopoietic stem cells (dependent claims 32-33) and the administered stem cells are genetically modified (dependent claim 93), and therefore they fall within the scope of claims 1-2, 4-9, 14-18 and 83 of the present application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments related in part to the above provisional double patenting rejections in the Amendment filed on 6/16/08 (pages 17-18) have been fully considered, but they are respectfully not found persuasive for the reasons discussed below.

Applicant argues basically that amended claims of the instant application are directed to methods for genetically altering a patient having a T cell disorder caused by HIV infection or methods for reducing or lowering HIV viral titer or infection of new cells in a patient; while claims of US Appl. 10/749,119 and U.S. Appl. 10/749,118 are directed to methods for increasing tolerance in a patient to a graft from an MHC-mismatched donor and methods for treating an autoimmune disease, respectively; and therefore the claims of the co-pending applications don not in any way teach, suggest or motivate one of ordinary skill to arrive at the currently amended claims of the present application. Additionally, the preamble of the instant claims is to be given effect.

The above rejected claims have nothing to do with a patient having HIV infection. The scope of the rejected claims is much broader and the claimed method of the present application comprises the same steps and starting materials as those of the co-pending applications. In fact, claims 1-2, 4-5, 7, 14-18 and 83 are linking claims that link a plurality of distinct inventions as already set forth in Office action dated 4/12/2007 (at least page 7). Additionally, the preamble of independent claims 1 and 83 simply recites "A method for genetically altering patient whose thymus has been at least in part deactivated" and "A method for improving uptake by the thymus of a patient of

genetically modified or exogenous cells", respectively, whose broad scopes encompass the scopes of the methods in the co-pending applications.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. *At the effective filing date of the present application, Greenstein, B.D. et al. (J. Endocr. 112:345-350, 1987; IDS) already taught that it is possible to regenerate the thymus of old rats treated with an analogue of LHRH without the need for surgical castration (see at least the abstract).*

2. *Kendall, M.D. et al. (Cell and Tissue Research 261:555-564, 1990) also demonstrated that reversal of ageing changes in the thymus of rats by chemical or surgical castration to obtain a significant increase in thymic weight and the reappearance of a well-defined cortex and medulla in ageing rats (see at least the abstract).*

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN/
Primary Examiner, Art Unit 1633